BRAIN RESEARCH 1531 (2013) 94–101

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Brain Research

Research Report

Negative emotional distraction on neural circuits for working memory in patients with posttraumatic stress disorder

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ARTICLE INFO

Article history:
Accepted 25 July 2013
Available online 2 August 2013

Keywords:
Posttraumatic stress disorder
Negative emotion interference
Working memory
Functional magnetic resonance imaging

ABSTRACT

Objective: To study the neural mechanism for the impact of negative emotional distraction on working memory in patients with posttraumatic stress disorder (PTSD) resulting from exposure to motor vehicle accidents.

Methods: Twenty PTSD patients and 20 healthy subjects were recruited. Event-related functional magnetic resonance imaging (fMRI) was used to investigate the effects of negative and neutral distractors on a delayed-response working memory task. All experiments were performed on a 3.0T MRI scanner, and the functional imaging data were analyzed using SPM8 software.

Results: The PTSD group showed poorer performance than the control group when the negative distractors were presented during the delay phase of working memory. The functional imaging indicated that, in the presence of negative relative to neutral distractors, the PTSD group showed higher activation in the emotion processing regions, including amygdala, precuneus and fusiform gyrus, but lower activation in the inferior frontal cortex, insula and left supramarginal gyrus than the control group.

Conclusion: Based on the results that activation in the PTSD patients in the presence of negative distractors increased in the emotion-related brain regions but decreased in the working memory-related brain regions, we may conclude that the neural basis of working memory is impaired by negative emotion in PTSD patients.

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0006-8993
http://dx.doi.org/10.1016/j.brainres.2013.07.042

1. Introduction

Posttraumatic stress disorder (PTSD) results from exposure to a traumatic event, such as a fight, violent crime, childhood abuse or motor vehicle accident, and is characterized by unique symptoms such as recurrent, involuntary recollection of the trauma in the form of intrusive thoughts, nightmares, or vivid sensory memories (Blake et al., 1995). It is notable that motor vehicle accidents are the leading cause of PTSD in the general population (Blanchard et al., 1994; Blanchard & Hickling, 2004). More importantly, rather than merely remembering it as a past event, PTSD sufferers seemingly relive the trauma with all its original intensity (McNally, 2006). Meanwhile, the trauma or trauma-related negative emotional stimuli may produce striking disturbances in cognition, especially in working memory. Previous studies have found that PTSD has been associated with marked cognitive deficits including working memory (Vasterling et al., 1998). However, the mechanism for the impact of negative emotional distraction on neural circuits for working memory in PTSD remains largely unknown.

In the recent years, a few functional neuroimaging studies have examined the neural basis of the impact of emotional distractors on working memory performance (Dolcos et al., 2006; McNally, 2006; Wessa et al., 2012; Fonzo et al., 2010). Some studies have shown that presenting emotional distractors during the delay interval evoked strong activity in typical emotion-processing regions of the brain (the amygdala and ventrolateral prefrontal cortex), while simultaneously evoking relative deactivation in the dorsal executive regions (the dorsolateral prefrontal cortex and lateral parietal cortex) and impairing working memory performance (Dolcos and McCarthy, 2006; Dolcos et al., 2006; Pannu Hayes et al., 2009). Aupperle et al. (2012) also found that activation is attenuated in the lateral prefrontal cortex but enhanced in the medial PFC, amygdala and insula during emotional anticipation. Activation was more positively correlated with the level of PTSD symptoms in the ventral frontolimbic regions (notably the ventromedial prefrontal cortex, inferior frontal gyrus, and ventral anterior cingulate gyrus) in the presence of negative stimuli than in the presence of neutral stimuli. Conversely, activation in performing executive tasks was negatively correlated with PTSD symptoms in the dorsal executive network, notably the middle frontal gyrus, dorsal anterior cingulate gyrus, and inferior parietal lobule (Morey et al., 2008). Additionally, the PTSD group showed neural activity markedly different from that of the control group, in response to task-irrelevant visual distractors. To be specific, in the PTSD group, enhanced activity in the ventral emotion-processing regions (the amygdala, ventrolateral prefrontal cortex, and fusiform gyrus) was associated with trauma distractors while activity in the dorsal executive regions (the dorsolateral prefrontal cortex and lateral parietal cortex) was associated with working memory, and attention was disrupted by the distractors independent of their trauma content (Morey et al., 2009). However, some other studies detected enhanced activation in the dorsal executive regions when emotional stimuli were presented as distractors before or during the task, potentially indicating compensatory activation to preserve goal-directed behavior (Wessa et al., 2012; Blair et al., 2008; Hart et al., 2010; Pereira et al., 2010).

Moreover, the functional neuroimaging studies of working memory have supported that the inferior frontal cortex plays a role in inhibitory processes (D'Esposito et al., 1999; Jha et al., 2004; Dolcos et al., 2006). The activity of the inferior frontal cortex is correlated with subjective ratings of distractibility for task-irrelevant emotional stimuli presented during the delay interval of a working memory task. In a former study, the participants who showed greater inferior-frontal-cortex activity in the presence of emotional distractors also rated themselves as less distracted, possibly as a result of engaging inhibitory processes that reduced the subjective impact of emotional distraction (Dolcos and McCarthy, 2006). Further studies extended the evidence from the studies of cognitive control of emotion that the inferior frontal cortex is involved not only in controlling the emotional response induced by potentially distracting emotional stimuli, but also in diminishing the negative impact of distracting emotions on ongoing cognitive processes (Dolcos et al., 2006). However, the precise role of the inferior frontal cortex in controlling the impact of negative emotional distraction on working memory in PTSD has not been firmly established.

In our previous study, we found significant decrease in cortical thickness in the left medial prefrontal cortex and anterior cingulate cortex in PTSD patients, indicating deficits in the working memory of PTSD patients (Xie et al., 2013). However, little is known about the neural mechanism for the impairment of working memory by negative emotional distraction. The mechanism has important implications for PTSD, as PTSD is characterized by increased susceptibility to emotional distraction. Therefore, the aim of the present study was to investigate the impact of negative emotional distractors on working memory in healthy controls and PTSD patients resulting from motor vehicle accidents using functional magnetic resonance imaging (fMRI) and to explore the neural mechanism for the impairment of working memory by negative emotional distractors in PTSD. We hypothesized that (1) the negative (relative to neutral) distractors would lead to increased activation in both groups, when more neural resources are devoted to working memory performance; (2) the negative emotional distractors would impair working memory performance in the PTSD group; (3) the negative emotional distractors would cause greater activation in the emotion-processing brain regions in the PTSD group than in the control group and impair the function of the inferior frontal cortex in the PTSD group.

2. Results

The PTSD patients and the control group were matched with respect to age, gender, and education duration; there was no significant difference in IQ between the two groups. The patients with PTSD had significantly higher CAPS scores than the control group (Table 1). According to the SCID, 3 subjects in the PTSD group met the DSM-IV diagnostic criteria for the depressive disorder. Among the control subjects, the SCID did not reveal any psychiatric disorders.

2.1. *Working memory performance*

The detectability scores (d-prime=Z(hit rate)−Z(false alarm rate)) of the control group were 4.63±0.14 for the neutral distractors and 4.48±0.16 for the negative distractors, and the detectability scores of the PTSD group were 4.16±0.23 for the neutral distractors and 3.04±0.21 for the negative distractors. To match the fMRI contrasts, the detectability scores were analyzed by two-way repeated measures analysis of variance in a group (PTSD, healthy control subjects) × factor (negative distractors, neutral distractors), revealing a significant main effect of group [$F(1,38)=31.561$, $p<0.001$] and main effect of distractor [$F(1,38)=11.803$, $p=0.001$], and a significant group × distractor interaction effect [$F(1,38)=6.805$, $p=0.013$]. Fisher's LSD tests showed that the detectability scores for the negative distractors significantly decreased more than those for the neutral distractors in the PTSD group ($p<0.05$), and the detectability scores for the negative distractors in the healthy control group were significantly higher than those in the PTSD group ($p<0.05$). There were no significant group differences when the neutral distractors were presented ($p>0.05$), and no significant differences in the control group ($p>0.05$) while the negative related to neutral distractors. Thus, the negative emotional distractors impaired the working-memory performance in the PTSD group, and the PTSD group showed poorer performance than the control group when the negative distractors were presented during the working-memory delay phase.

Simple linear regression analyses showed a negative correlation between the detectability scores of the PTSD group in the presence of negative distractors and clinical CAPS scores ($R^2=0.475$, $p=.03$) but no correlation between the detectability scores in the presence of the neutral distractors and clinical CAPS scores. No correlation was found between the detectability scores and clinical CAPS scores in the control group.

Table 1 – Demographic and clinical features of the two groups.

Variable	PTSD ($n=20$)	Controls ($n=20$)	p value*
Mean age in years (SD)	32.92 (8.48)	31.53 (7.43)	0.451
Gender	Male (13), Female (7)	Male (14), Female (6)	0.736
Mean education in years (SD)	11.20 (3.80)	13.00 (2.20)	0.374
IQ (SD)	98.20 (5.50)	103.20 (6.30)	0.242
CAPS total score, mean (SD)	52.33 (9.44)	8.26 (9.31)	0.000

CAPS, Clinician-Administered PTSD Scale (range, 0–136).
* p values were calculated by x^2 statistics for categorical measures and 2-tailed t statistics for continuous measures.

2.2. *fMRI results*

For a whole-brain analysis examining BOLD response to the negative vs. neutral distraction, both the healthy control group and the PTSD group showed similarly activated brain regions (Fig. 2). As seen in Fig. 2, increased activation was found in the amygdala, putamen, inferior frontal cortex, hippocampus, thalamus, fusiform gyrus, superior parietal lobe and occipital lobe, and no decreased activation was found.

Compared with the control group using the t maps of negative vs. neutral distractors, the PTSD group showed greater activation in the left amygdala and superior parietal lobe, bilateral fusiform gyrus and superior temporal gyrus, and precuneus, and simultaneously lower brain activity in the inferior frontal cortex, right insula, and left supramarginal gyrus during the delay phase (Fig. 3, Table 2).

Simple linear regression analyses revealed that clinical CAPS scores of the PTSD group were positively correlated with the activation of the fusiform gyrus ($R^2=0.423$, $p=.04$) and with the left amygdale ($R^2=0.482$, $p=.03$), and negatively correlated with the activation of the inferior frontal cortex ($R^2=0.494$, $p=.02$), but no correlation with the activation of the other ROI.

3. Discussion

The present study examined the neural activity of the control and PTSD groups in response to neutral and trauma-related negative stimuli presented as task-irrelevant distractors during

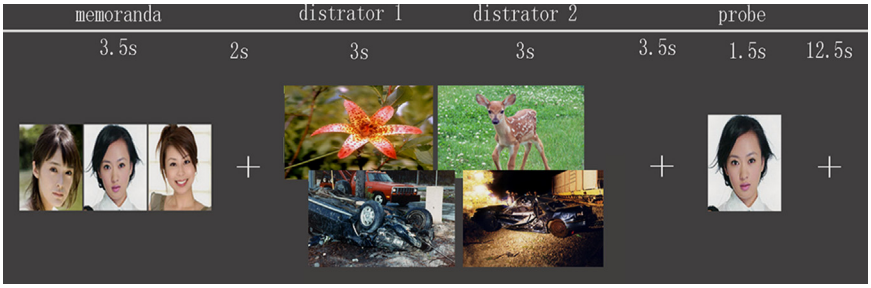

Fig. 1 – Diagram of the working memory task showing the event order and trial types. The subjects were instructed to encode the memoranda (3 faces) and had to actively maintain them in working memory during the delay phase while looking at the distractors. During the retrieval phase, the subjects were required to press a response button to indicate whether the probe (single-face) was part of the memoranda. Two categories of trials were presented during the working memory delay phase, defined by the type of distractors, (i) negative images or (ii) neutral images. Each trial contained two distractors from the same category that were presented, consecutively, for 3 s each.

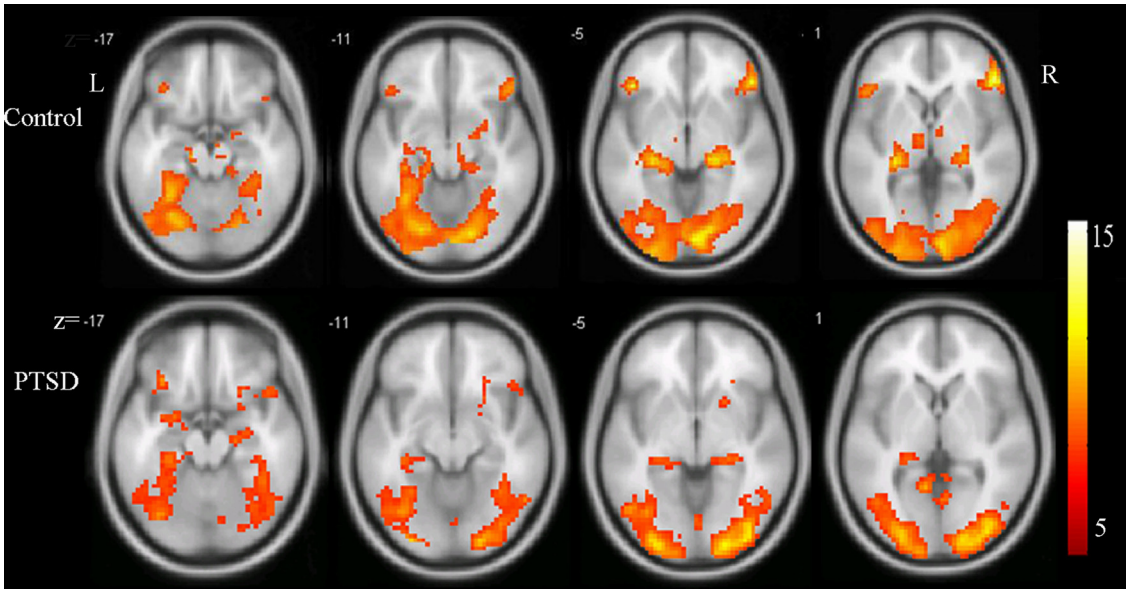

Fig. 2 – Activated regions in the negative vs. neutral distraction in the healthy control group and PTSD group, respectively. The numbers beside the brain images indicate the location on the Z axis. The color bar indicates T-score. The warm color indicates increased activation.

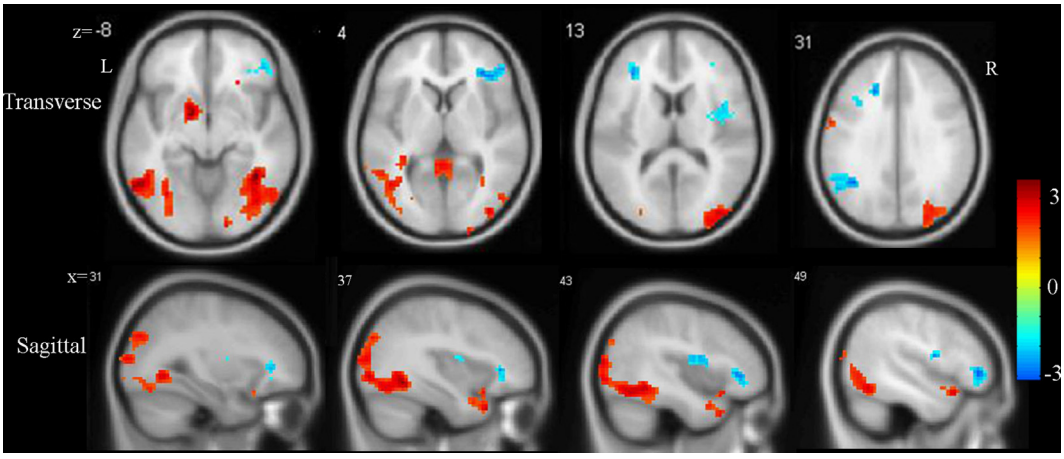

Fig. 3 – Abnormal activation of regions in the PTSD group compared to the control group for negative relative to neutral distractors. The numbers beside the brain images indicate the location on the Z axis (transverse) and X axis (sagittal). The color bar indicates *T*-score. The warm color indicates increased activation, and cold color decreased activation.

Table 2 – Significant clusters identified in PTSD patients compared with controls (negative vs. neutral distractors).

	Anatomic definition	Brodmann area	Voxels	MNI coordinates		
				X	Y	Z
ptsd > control	Left fusiform gyrus	37	372	−36	−61	−11
	Right fusiform gyrus	37	218	34	−64	−10
	Precuneus	29	45	−1	−45	5
	Left amygdala	–	29	−18	−1	−14
	Left superior parietal lobe	39	76	−20	−63	64
	Left superior temporal gyrus	38	58	−28	6	−27
	Right superior temporal gyrus	38	61	41	11	−28
ptsd < control	Left supramarginal gyrus	40	25	−52	−54	31
	Left frontal operculum	44	36	−36	18	30
	Left frontal triangle	45	44	−31	37	12
	Right frontal triangle	45	39	41	34	3
	Right anterior insula	13	52	44	2	13

the delay phase of a working memory task, and the results showed increased activity in the amygdala, putamen, inferior frontal cortex, hippocampus, thalamus, fusiform gyrus, superior parietal lobe and occipital lobe in the presence of negative compared to neutral distractors in both groups. The results supported our hypothesis that the negative relative to neutral distractors would enhance activation in both groups, suggesting that more neural resources might be devoted to working memory performance in response to negative distractors. No significant differences was found in the detectability scores for the negative related to neutral distractors in the control group, suggesting that the working memory regions such as the hippocampus, inferior frontal cortex and parietal cortex play an important role in keeping working memory from negative mood disturbance. As a compensatory mechanism for dealing with increased emotional interference, the task-specific activation is boosted in order to overcome the distraction effect (Wessa et al., 2007; Dichter et al., 2009; Phillips et al., 2008). This result is also consistent with some previous studies which found enhanced activation in dorsal 'cognitive' brain regions (Wessa et al., 2012; Blair et al., 2008; Hart et al., 2010; Pereira et al., 2010), but different from some others which reported that negative emotional distractors led to decreased activation of the working memory regions (the dorsolateral PFC and lateral parietal cortex) (Dolcos and McCarthy, 2006; Dolcos et al., 2006; Morey et al., 2009). We speculated that the activation reduction found in the latter studies might reflect a different cognitive process (Wessa et al., 2012).

More importantly, although both groups showed enhanced activation in response to negative distractors, in the presence of negative relative to neutral distractors, the activation of the PTSD group was higher than that of the control group in the emotion processing regions (including the fusiform gyrus and amygdale) but lower than that of the control group in the inferior frontal cortex, insula and left supramarginal gyrus. At the same time, the PTSD group showed poorer performance than the control group when the negative distractors were presented during the working-memory delay phase, and there was a negative correlation between the detectability scores of the PTSD group in response to the negative distractors and the clinical CAPS scores ($R^2=0.475$, $p=.03$). These results supported our hypotheses that negative distractors would cause greater activation in the emotion-processing regions in the PTSD group than in the control group and impair working-memory performance in the PTSD group.

Simple linear regression analyses showed that the clinical CAPS scores of the PTSD group were positively correlated with the activation of the fusiform gyrus and amygdala. In PTSD patients, the fusiform gyrus, a high-order visual cortex, has been found showing strong response to images with trauma-related content (Hendler et al., 2003), which is consistent with our findings. In addition, the increased activation in the fusiform gyrus and amygdala might also support the notion that traumatic and stressful events could modify visual processing by the limbic system (e.g. the amygdala) (Hendler et al., 2003). Previous human neuroimaging studies have found that brain regions associated with emotion processing, especially the amygdala, are activated in response to negative stimuli (Irwin et al., 1996; Mather et al., 2004). Recently, Pannu Hayes et al. (2009) also reported that greater PTSD symptomatology showed enhanced neural activity in the ventral-limbic regions in response to emotional stimuli. Our results of increased activation in emotion-processing regions due to negative distractors indicated that emotion regulation was disrupted in the PTSD patients, since trauma exposure itself might impede the ability to control emotional responses to negative stimuli (e.g. pictures depicting the scenes of motor vehicle accidents in this study) (New et al., 2009).

Although the negative distractors were task-irrelevant, the PTSD patients seemed to be more susceptible to those distractors than the healthy controls, which is reflected not only in their poorer performance of the working memory tasks, but also in the reduced activation in their working memory-related brain regions. The inferior frontal cortex serves working memory by maintaining object information and simultaneous inhibiting distracting information (Dolcos et al., 2006; Ranganath and D'Esposito, 2005). Simple linear regression analyses also showed that the clinical CAPS scores of the PTSD group were negatively correlated with the activation of the inferior frontal cortex. The reduced activation in this region suggests that PTSD could not diminish the negative impact of distracting emotions on ongoing cognitive processes, resulting in the poorer performance of the PTSD group when the negative and neutral distractors were presented during the working-memory delay phase. Recent functional neuroimaging studies of working memory have also supported that the inferior frontal cortex plays a role in inhibitory processes, in that experimental conditions requiring the highest level of inhibition produced the highest level of activity in the inferior frontal cortex (Jha et al., 2004; Jonides et al., 1998). The fact that the control group showed greater activity of the inferior frontal cortex in the presence of emotional distractors in this study is probably a result of engaging inhibitory processes to reduce the emotional distraction. We speculated that greater activation in working-memory regions might act as a compensatory mechanism for dealing with greater emotional interference. Therefore, our findings indicate that PTSD patients could not invoke the compensatory mechanism to regulate their brain activity and perform ongoing cognitive tasks in the presence of negative distractors. In addition, the decreased activation in the inferior frontal cortex and supramarginal gyrus (a portion of the parietal lobe) indicated disrupted recruitment of the fronto-parietal regions, supporting that emotional responsiveness could interfere with the recruitment of regions associated with top-down attentional control (Blair et al., 2013). The present study might help reveal the neural mechanism for negative emotional distraction impairing working memory.

It's worth noting that the activation in the right anterior insula was decreased in PTSD patients. This finding is not consistent with most previous results revealing that PTSD patients show exaggerated activation during anticipation and processing of emotional stimuli (Etkin and Wager, 2007; Simmons et al., 2008; Felmingham et al., 2010; Fonzo et al., 2010). There might be two possible reasons: (1) different locations of insula activation (anterior vs. posterior; left vs. right); (2) different task stimuli (emotional stimuli vs. working memory with emotional distraction). However, in a study of

cognitive activation paradigm, Shin et al. (2001) found reduced fMRI signal in right anterior insula in the PTSD group. Simmons et al. (2009) investigated the neural networks during affective set-shifting in PTSD and also found that PTSD group showed significantly less activation in the right anterior insula than the controls, indicating the inability of PTSD patients to preemptively modify interoceptive state. The right anterior insula is centrally involved in affecting changes in interceptive state (Craig, 2003; Paulus and Stein, 2006). Therefore, we speculated that decreased activation of the right anterior insula affected the ability of PTSD patients to adjust interoceptive state, and then impeded the implement of subsequent working memory task.

Some limitations of the present study are noteworthy. First, the sample size is relatively small (especially for regression analyses conducted solely within the PTSD group), which may have limited our understanding of the findings and, therefore, warrants further replication with a larger sample. Second, we did not consider thoroughly in processing the data, as only correct trials were included in the analysis, neglecting the different types of regressors adopted. It may be more accurate to model the probe responses with two or three different regressors: new, old, and incorrect ones. Last, the control group only consists of healthy participants for investigating the neural mechanism for the impairment of working memory by negative emotion distraction in PTSD patients. Although we tried our best to exclude the patients with head injury from the PTSD group, a possibility exists that mild traumatic brain injury (mTBI) might have some influence on our results. Comparative analysis involving non-PTSD patients with traffic trauma rehabilitation would help us better understand the pathomechanism of PTSD.

4. Experimental procedures

4.1. Subjects

The subjects in the present study also participated in our previous study (Xie et al., 2013). A total of 20 PTSD patients (range, 18–40 years; mean, 32.92 years) who had been involved in motor vehicle accidents were recruited from Southwest Hospital, the Third Military Medical University. Diagnosis of PTSD was confirmed according to the Clinician-Administered PTSD Scale for DSM-IV (CAPS-DX) (Blake et al., 1995). Twenty healthy controls (range, 20–38 years; mean, 31.53 years) individually matched by age, gender and duration of education were consecutively recruited from the community. Inclusion criteria for all the subjects were right-handedness and an IQ>80 as assessed by the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV). Patients had no Axis I psychiatric history other than depression on the Structured Clinical Interview for DSM-IV (SCID) Axis I Disorders, whereas controls were free from Axis I disorder on the SCID (First, 1997). Exclusion criteria for both groups were contraindications for MRI and other neuropsychiatric disorders, such as schizophrenia, mental retardation, epilepsy, and head injury (i.e., abnormalities on CT or MRI, neurological abnormality during Emergency Department evaluation, posttraumatic amnesia, loss of consciousness for more than 5 min during the accident, or Glasgow Coma Score less than 14). All the PTSD patients were diagnosed for the first time during the investigation and had not taken psychotropic medication.

4.2. Ethical statement

This research was conducted in line with the International ethical guidelines for biomedical research involving human subjects (Macrae, 2007), and approved by the Ethics Committee of the Third Military Medical University. All the participants have signed the informed consent after receiving a complete description of the study.

4.3. Experimental stimuli and design

Subjects completed in the presence of distraction a similar version of the working memory task used in previous studies (Dolcos and McCarthy, 2006; Morey et al., 2009). Each trial consisted of an encoding phase, a delay phase with emotional (trauma-related) and non-emotional visual distractors, and a retrieval phase for an overall epoch duration of 29 s (Fig. 1). The memoranda consisted of sets of three female faces presented for 3.5 s, and the distractors consisted of (i) two pictures depicting motor vehicle accident scenes (as negative distractors), or (ii) two pictures depicting natural scenes unrelated to motor vehicle (as neutral distractors), presented for 3 s each. The neutral distractors served as a control condition. During the retrieval phase, a single-face probe was presented requiring a button response to indicate its presence (Old) or absence (New) in the three-face memoranda (50% probes were old and 50% new). Subjects were instructed to attend to the memoranda and distractors, and responded with an Old or New judgment to the probes. Each probe was followed by a fixation cross for 12.5 s to allow the hemodynamic response to return to the baseline. Subjects viewed 20 trials per stimulus type randomized across 5 runs; there was no repetition in the memoranda, distractors, or probes.

The pictures as negative and neutral distractors were selected from the International Affective Picture System (IAPS) (Lang et al., 1997). According to the arousal and valence scales from IAPS, the arousal and valence scales of the negative distractors were $6.02 \pm 0.43/2.18 \pm 0.47$, and the neutral distractors $4.79 \pm 0.76/5.40 \pm 1.10$.

4.4. Image acquisition

All the experiments were performed on a 3.0T Siemens MRI scanner (Trio, Siemens Medical Erlangen, Germany). Foam padding was used to minimize head motion for all the subjects. The EPI fMRI data were acquired using the following parameters: TR/TE/FA 2000 ms/30 ms/90°, 36 transverse slices, thickness of 3.0 mm, and FOV of 220×220 mm. T1-weighted images in the sagittal plane of all the subjects were acquired using a 3D MPRAGE sequence with TR/1900 ms, TE/2.34 ms, flip angle/7°, FOV/256×256, and slice thickness/1 mm.

4.5. *Image processing and analysis*

Image preprocessing and statistical analysis were performed using SPM8 software (http://fil.ion.ucl.ac.uk.spm/). For each subject, standard steps for preprocessing the EPI images were taken, including correction for slice timing and head motion, registration to a high-resolution anatomical image, spatial normalization using the Montreal Neurological Institute (MNI) echo-planar imaging template, and smoothing using a Gaussian kernel of 8-mm full-width at half maximum. A temporal high-pass filter with a cutoff phase of 128 s was also applied, followed by the whole-brain voxel-based GLM at the single-subject level to estimate signal change associated with the conditions of interest (e.g. negative distractors during the working-memory delay phase) using six motion parameters as covariates of no interest. Specifically, one regressor was used to model the encoding phase (memeoranda) with a boxcar function of 3.5-s duration; two regressors with 6-s boxcar functions were used to model the working-memory delay phase for the negative and neutral distractor conditions; and one regressor was used to model probe responses with delta functions. The 5 runs of EPI data were analyzed together, and one regressor per distractor type (neutral or negative) was created for all 5 runs together. For individual analysis, the fMRI signal (the beta values) was selectively averaged in each subject as a function of distraction (i.e., negative, neutral pictures) using custom MATLAB software, and pairwise *t* statistics for the contrast of interest (negative vs neutral distractors) were calculated for each subject. Individual analysis produced whole-brain average and activation t maps for contrast of interest (negative vs neutral distractors).

The outputs of the individual analysis were used as inputs for second-level-group analysis using two-sample, two-tailed t-tests. An intensity threshold of $p<0.01$ and an extent threshold of 20 contiguous voxels were used for correction during multiple voxel comparisons. The t-map was set at a corrected threshold of $p<0.05$ (combined height threshold $p<0.01$ and a minimum cluster size of 20 voxels), using the AlphaSim program in the REST software (http://www.rest-fmri.net/forum/REST_V1.8), which applied Monte Carlo simulation to calculating the probability of false positive detection by considering both the individual voxel probability thresholding and cluster size. Next, activation of the region of interest (ROI) was calculated in each of the PTSD patients that increased or decreased than the control group.

4.6. *Statistical analysis*

The detectability scores (d-prime=Z(hit rate)−Z(false alarm rate)) of each subject were calculated by Excel 2007, and analyzed by two-way repeated measures analysis of variance (ANOVA) using SPSS for Windows (v17.0, SPSS Inc, Chicago, Illinois, USA). Simple linear regression analyses were performed to investigate the relationship between the detectability scores (independent variable) and clinical CAPS scores (dependent variable). Two-tailed x^2 test was performed to compare the difference between the two groups. Meanwhile, simple linear regression analyses were performed to investigate the relationship between the activation of ROI (independent variable) and clinical CAPS scores (dependent variable) of the PTSD patients. All the results were quoted as 2-sided *p* values. $p<0.05$ was considered statistically significant.

Acknowledgments

This study was sponsored by the National Natural Science Foundation of China (Grant number 30870696), the Starting Funds of Third Military University (TMMU2009XHG01), and the Natural Science Foundation of Chongqing (CSTC2009BB5019).

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